Appl. No. : 10/036,150
Filed : December 26, 2001

REMARKS

Claims 22-30, 32-34 and 38-41 are pending. Claim 35 is cancelled without prejudice to future prosecution. Claims 22-27 and 30 have been amended as set forth above to remove the references to the extracellular domain. Support for the amendment is found in Figures 19-20, which provide the nucleotide sequence encoding PRO4405 and specify a transmembrane domain for the PRO polypeptide. Support is also found in the specification at page 66, lines 21-25 which recites:

> Another aspect [of] the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence encoding a PRO polypeptide which is either transmembrane domain deleted or transmembrane domain inactivated, or is complementary to such encoding nucleotide sequence, wherein the transmembrane domain(s) of such polypeptide are disclosed herein. Therefore, soluble extracellular domains of the herein described PRO polypeptides are contemplated.

Also, Claims 22-25 have been amended to recite 95%, 96%, 97% and 98% nucleic acid sequence identity, respectively. Support for the amendment is found for example, in the specification at page 66, lines 15-17. No new matter is added by the amendments and the claims are fully supported by the specification as originally filed.

Applicants respond below to the remaining rejections raised by the Examiner in the Office Action mailed September 12, 2005. For the reasons set forth below, Applicants respectfully traverse.

Rejections under 35 U.S.C. §112, first paragraph – Written Description/New Matter

The Examiner continues to reject Claims 22-27, 30 and 35-41 under 35 U.S.C. §112, first paragraph as lacking an adequate written description. The Examiner argues that redefining the extracellular domain as amino acids 77-310 constitutes new matter.

As set forth above, Claims 22-27 and 30 have been amended to remove reference to the "extracellular domain," thereby obviating the Examiner's rejection insofar as it relates to the recitation of the extracellular domain of SEQ ID NO:45. Specific recitation of the fragment sequence encoding amino acids 77-310 of SEQ ID NO:45 is supported by Figure 20 which lists the transmembrane domain as being amino acids 58-76 and by the specification, which states that an aspect of the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence encoding a PRO polypeptide which does not have a transmembrane domain. *See*

specification at page 66, lines 21-25. Therefore, reconsideration and withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. §112, first paragraph – Written Description

The Examiner continues to reject Claims 22-27, 30, 35 and 38-41 under 35 U.S.C. §112, first paragraph as lacking written description for the reasons previously of record and for the following additional reasons. The Examiner asserts that the claims fail to recite that the claimed nucleic acids are isolated "human" nucleic acids. The Examiner also continues to argue that the holdings in *Fiers v. Revel*, *Fiddes v. Baird*, *Regents of the Univ. of Cal. v. Ely Lilly and Co.*, and *Vas-Cath* are applicable to this case. Furthermore, the Examiner refers to Claim 22(c) to argue that the claims do not define an open reading frame in a definable nucleic acid molecule, but instead encompass undescribed nucleotide sequences. The Examiner argues that the claims are distinguishable from Example 14 of the written description training materials. In particular, the Examiner argues that, in contrast to Example 14, the claims were not limited to a "nucleic acid having at least 95% sequence identity ... encoding [a] polypeptide," as illustrated in Example 14, in which a reasonable correlation between structure and function may be possible for a claimed genus. Applicants respectfully disagree.

Applicant has amended Claims 22-26 to recite at least 95%, 96%, 97%, 98% and 99% sequence identity to several nucleic acid sequences related to SEQ ID NOs:44-45. The nucleic acid variants must also satisfy the limitation "wherein said isolated nucleic acid encodes a polypeptide that has the ability to induce chondrocyte redifferentiation."

In view of this, Applicants maintain that the variant claims recite sufficient distinguishing characteristics for the claimed genus of nucleic acids, including nucleic acids from species other than humans. Based upon the detailed description of the cloning and expression of nucleic acid variants and variants of PRO4405 in the specification, the description of the assay in Example 36, the actual reduction to practice of sequences SEQ ID NOs: 44 and 45, and the functional recitation in the instant claims, Applicants submit that one of skill in the art would know that Applicants possessed the invention as claimed in the instant claims.

Applicants again assert that the pending claims are analogous to the claims discussed in Example 14 of the written description training materials. For reasons similar to those expressed in Example 14 of the training materials, the written description requirement should be deemed

satisfied for the instant claims. A copy of Example 14 from the training materials is included herewith as Exhibit 1 for the convenience of the Examiner. In Example 14, the written description requirement was found to be satisfied for claims relating to polypeptides (1) having a percentage of homology (95%) to a particular sequence and (2) possessing a particular function/catalytic activity. The claims were considered fully described even though the applicant had not made any variants and even though only a single representative species was disclosed. Example 14 notes that the procedures for making variants were conventional in the art and that an assay was described in the specification which will identify other proteins having the claimed catalytic activity.

Similarly, in the instant case the pending claims recite a genus of nucleic acids without substantial variation. As in Example 14 of the training materials, the claims (1) require a high percentage of sequence identity to the disclosed sequence of SEQ ID NO:44 or to a sequence encoding SEQ ID NO:45, and (2) require that the variant sequences encode a polypeptide that has a specific functional activity, namely, the ability to induce chondrocyte redifferentiation. Furthermore, the specification describes how to make the claimed nucleic acid variants. In addition, Example 36 of the specification on page 166 discloses how to test to determine if a polypeptide has the ability to induce chondrocyte redifferentiation. Thus, like Example 14, one of skill in the art would conclude that Applicants "were in possession of the necessary common attributes possessed by members of the genus." Therefore, Applicants assert that the written description requirement of § 112 is satisfied for all of the pending claims.

Finally, for the reasons set forth in the previous response dated June 23, 2005, Applicants again insist that the instant claims and facts are distinguishable from those at issue in *Fiers v. Revel*, *Fiddes v. Baird*, *Regents of the Univ. of Cal. v. Ely Lilly and Co.*, and *Vas-Cath*. None of the cited cases is closely analogous to the instant case, and particularly not as analogous as Example 14 of the training materials for Examiners. For example, none of the disputed cases sought to claim sequences based upon identity or homology to a disclosed sequence in combination with a functional limitation.

For the reasons set forth above, Applicants assert that one of ordinary skill in the art would recognize that Applicants possessed the claimed subject matter at the time of filing the instant application. Hence, Applicants respectfully request that the Examiner reconsider and withdraw the written description rejection under 35 U.S.C. §112.

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Rejections under 35 U.S.C. §102 – Anticipation

The Examiner rejects Claim 35 under 35 U.S.C. § 102(b) as being anticipated by Adams et al. (clone EST70856; Accession No. AA361388; April 21, 1997). According to the Examiner Adams et al. teach a nucleic acid that is 98% identical to nucleotides 144-397 of SEQ ID NO:44 such that it would hybridize to the claimed sequences, and that the sequence encodes enough structure to inherently possess the recited functional language.

As discussed above, Claim 35 has been cancelled without prejudice. Therefore, the instant rejection is moot.

Conclusion

The present application is believed to be in condition for allowance, and an early action to that effect is respectfully solicited. Applicants invite the Examiner to call the undersigned if any issues may be resolved through a telephonic conversation.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 12/9/05

By: _____

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